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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/635,048	08/04/2003	Jallal Messadek	31927-CIP2	6961
7590 HOVEY WILLIAMS LLP Suite 400 2405 Grand Boulevard Kansas City, MO 64108		09/20/2007	EXAMINER BETTON, TIMOTHY E	
			ART UNIT 1614	PAPER NUMBER
			MAIL DATE 09/20/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/635,048	MESSADEK, JALLAL
	<b>Examiner</b>	<b>Art Unit</b>
	Timothy E. Betton	1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 20 June 2007.  
 2a) This action is FINAL.                  2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-25 and 27-42 is/are pending in the application.  
 4a) Of the above claim(s) 1-13 and 31-41 is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 14-25,27-30 and 42 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement(s) (PTO/SB/08)  
     Paper No(s)/Mail Date See Continuation Sheet.
- 4) Interview Summary (PTO-413)  
     Paper No(s)/Mail Date. \_\_\_\_\_.  
 5) Notice of Informal Patent Application  
 6) Other: \_\_\_\_\_.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :7/19/2007 and 6/20/2007 5 sheets.

**DETAILED ACTION**

Applicants' arguments, filed 20 June 2007, have been fully considered but they are not deemed to be persuasive.

Applicants argue that the primary references (the Cubicciotti references) cited by the Examiner do not teach or suggest the use of glycine betaine or any betaine derivative, as conceded by the Examiner at the bottom of page 6 of the Office Action. Rather, the Examiner cited the Cubicciotti references for their alleged teachings of drug delivery systems, and then points to the Malamud et al. and Murphy et al. patents to supplement this significant shortcoming in the teachings of the Cubicciotti references. The Applicant submits that the art of record does not teach or suggest the claimed controlled release system that comprises glycine betaine as is required to establish a *prima facie* case of obviousness. The Examiner points to column 5, lines 38 and 45 of Malamud et al. for the alleged teaching of betaine or a betaine derivative and glycine derivative." The Applicant respectfully disagrees with the characterization of this teaching.

However, the rejection based on 35 USC 103 (a) is maintained for the reasons already of record. The Amarisinghe et al. reference has been withdrawn.

The Cubicciotti et al. references teach the same elements of claimed invention with the exception of glycine and/or its derivatives. However, Malamud et al. suggest the motivation to combine with Cubicciotti et al., because Malamud et al. teach use with a betaine derivative and a glycine derivative in a remotely controlled drug delivery system. Malamud et al. teaches a predetermined dose of a drug for administration.

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Murphy et al. teach the controlled release of active drug substances in various compartments of the mammal in need of such treatment. Murphy also teaches administration with glycine or derivatives thereof.

Further, in the instant claims or specification, the applicant cites no definitive exclusion of compounds directed solely to glycine betaine. The Applicants specifically cite in instant claims 1, 19 and 27 "*an effective amount of an active compound selected from the group consisting of glycine betaine, [...], precursors, [...].*" The term *precursor* is not defined and is not explained in the instant specification as excluding any other derivatives of glycine betaine.

Applicants have no support with which to suggest that glycine betaine is the preferred embodiment in view of the claimed invention at the exclusion of its derivatives and mixtures thereof as disclosed.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

***Claim Rejection- 35 USC –112-1<sup>st</sup> paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-25, 27-30, and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains

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subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Instant claims 14-25, 27-30, and 42 disclose *glycine betaine, pharmaceutically acceptable salts thereof, precursors thereof, and mixtures thereof*. Embodiments containing explanations directed toward glycine betaine are present. However, the claimed invention discloses [...], *precursors thereof, [...]..*, of which the specification is absent of support commensurate with claimed invention.

Specifically, *precursors* (any compound derived from related genus) is not identified nor is there at least a representative set discussed such that one of skill in the art would know what compounds would be considered *precursors*. There is no requisite limitation in the claims or specification stating as to how far from glycine betaine one of ordinary skill may extrapolate in consideration of a precursor.

***Claim Rejection-35 USC§ 103(a)***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 14-25 and 27-30 are rejected under 35 U.S.C. 103(a) as being obvious and therefore unpatentable over Cubicciotti, R. (USPN 6287765 and PGPUB US 20020334757) in view of Malamud et al. (USPN 5928195), and Murphy et al. (USPN 6399785). The applied references have a common claimed invention and/or method steps with the instant application.

The instant claims are drawn to a controlled release pharmaceutical system suitable for delivering after administration in a time-controlled manner to the bloodstream of a mammal, comprising an effective amount of an active compound selected from the group consisting of a compound of disclosed formula [glycine betaine], or a pharmaceutically acceptable salt thereof; precursors thereof, and mixtures thereof.

Cubicciotti et al. teach multimolecular devices and drug delivery systems prepared from synthetic heteropolymers, heteropolymeric discrete structures, multivalent heteropolymeric hybrid structures, aptameric multimolecular devices, multivalent imprints, tethered specific recognition devices, paired specific recognition devices, nonaptameric multimolecular devices and immobilized multimolecular structures are provided, including molecular adsorbents and multimolecular adherents, adhesives, transducers, switches, sensors and delivery systems. Methods for selecting single synthetic nucleotides, shape-specific probes and specifically attractive surfaces for use in these multimolecular devices are also provided. In addition, paired nucleotide-nonnucleotide mapping libraries for transposition of selected populations of selected

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nonoligonucleotide molecules into selected populations of replicatable nucleotide sequences are described. Further Cubicciotti et al. teach controlled release pharmaceutical system suitable to delivering (Abstract, column 38, lines 8-37) [...] to bloodstream (column 147, line 60), comprising an effective amount of an active compound or derivative thereof (column 183, line 61). Instant claim 15 is obvious over Cubicciotti et al. in regard to oral and transdermal controlled release devices/preparations. Referenced patent discloses a time-controlled transdermal application (column 50, line 57) and time-controlled oral application (column 107, line 41). Instant claim 17 is obvious over Cubicciotti et al. in regard to the disclosure: electronic element selected from the group consisting of an electronic device or/and chip. Referenced patent discloses numerous disclosures of chips and derivatives thereof (column 4, line 2; column 13, line 60; column 59, line 7). Instant claim 19 is obvious over above-referenced PGPUB US 20020034757 A1 in regard to treating a condition, reducing the incidence, or reducing the severity of a condition, whereby said condition, is blood flow disturbances, thrombosis, thromboembolic disorders. Referenced PGPUB discloses vascular thrombotic events and thrombosis (Section [808]).

Cubicciotti et al. does not teach the use with glycine betaine or any betaine derivative thereof.

However, the Examiner refers to Malamud et al., which does teach the use with betaine or a betaine derivative and/or a glycine derivative (column 5, lines 38 and 45,

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respectively) in a remotely controlled drug delivery device, which administers a dose of said drug, agent or microbicide using a gas pressure delivery system. The device stores multiple doses of the drug or agent. A toroid shaped housing includes three chambers, a gas chamber containing a pressurized gas, a drug storage chamber containing the drug or agent, and an expandable chamber for delivering the drug from the drug storage. The device includes an electronic controller for opening a valve connecting the gas chamber to the expandable chamber for a predetermined period of time in order to deliver a predetermined dose of the drug. The controller communicates with a remote control device via radio frequency. The remote control device sends a signal to the controller, which causes a dose to be delivered. The controller returns a signal to the remote control device indicating that the dose has been delivered and a signal indicating when the device needs to be removed for maintenance. The device may be used in any body cavity to deliver any desired type of drug. Specifically in subject claim 8 and column 5, line 37 of instant patent, there is the direct disclosure of a derivative of betaine for use in controlled drug delivery device. Malamud et al., does not teach the identical specifications of the electronic element as disclosed in instant claims but does disclose a form of gas pressure delivery system. Malamud et al. further makes obvious the motivation to combine the use of betaine and derivatives thereof for use in a pharmaceutical delivery system. The motivation is further made obvious by references in view of Murphy et al. (USPN 6399785).

In view of Murphy et al. (USPN 6399785), the patented reference teaches the use of a pharmaceutical delivery system and glycine and/or derivatives by referenced disclosure: the controlled release of active drug substances into the gastrointestinal, circulatory, lymphatic, cerebrospinal, synovial fluid, biliary, within the aqueous of the eye, or in other systems in the body of a [mammal] effected in a continuous and constant manner. (column 28, lines 1-18).

Further, claims 23-25, 27, and 28 are rejected under 35 USC 103(a) as being obvious over Cubicciotti et al. in view of Malamud et al.

Malamud et al. teaches an intravaginal microbicide device which is administered by way of a gas pressure delivery system. The device includes an electronic chamber for opening a valve connecting the gas Chamber to the expandable chamber for a predetermined period of time in order to deliver a predetermined dose of the drug. The controller communicates with a remote control device via radio frequency. Referenced patent teaches that the dispersion time may vary depending on the drug used and the location of the drug delivery device 12. In the preferred embodiment, it is preferred that a delivered dose of the drug remains effective for at least six to eight hours [...] (column 5, lines 53-57).

Instant claims disclose a system adapted for controlling the release of an effective amount of a compound for at least ranges comprising at least 180 minutes to 360 minutes. The Malamud et al teaching of *at least six to eight hours* encompasses the

ranges of the subject claims. The delivery/dispersion methods are not identical, however, a common system of interval-based administration is practiced. The disclosed ranges of instant claims disclose specific values in regard to the related, however, a general teaching drawn to a predetermined period of time in the referenced patent.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the devices of Cubicciotti et al. and Murphy et al. and combine with Malamud et al. to include the administration of glycine betaine in a pharmacy delivery system.

### **Conclusion**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic

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Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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